

INTERACTIONS BETWEEN THE AUTONOMIC AND CENTRAL NERVOUS SYSTEM DURING THE FIRST SLOW-SLEEP CYCLE

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ABSTRACT

Objective: To characterise the different sleep states and look for the spatial and frequential changes in the different regions of the brain during the awake-slow sleep transition and the interactions between the cardiac activity and respiration and also to study the relationship between the left and right cerebral hemispheres during sleep by Cross correlation of the momentary band power time series' of EEG, Heart-Rate Variability (HRV) and Respiration signals for the different frequency bands for each sleep state and their Moments by Linear Regression analysis.

Results and Conclusions: Subdivision of alpha frequency band into two (ie., alpha1 and alpha2). Transition from one state to another-linear regression analysis. Parasympathetic – sympathetic balance during the wake-sleep cycle: seen from the mean normalised cardiac activity.

Keywords : EEG, ECG, Respiration, Cross-correlation, Momentary band power, Amplitude spectrum, Time-frequency analysis, Moments

1. INTRODUCTION

The interactions between the ANS and the CNS can be studied by the influence of heart activity on the brain and respiration during different states of the wake-sleep cycle. In our analysis, we studied the interactions of the different physiological processes during the first wake-slow wave sleep cycle and characterised the different states of sleep by the process of cross correlation.

The main perspective of our study was to characterise the different states of sleep and to investigate the spatial and frequential changes in different regions of the brain during the sleep transition from awake to deep sleep (or slow wave sleep) and the influence or the interactions between the respiration and heart activity and also between the left and right hemispheres of the brain.

2. METHODS AND MATERIALS

Data Acquisition:

Polysomnography (recorded for one whole night) of eight children in the age group of 6-9 years were recorded. The selected children were normal and those with severe pathological conditions were not considered. For our detailed analysis, we used only the first complete awake-slow sleep cycle.

Primary measures (EEG, EOG, EMG, ECG and Respiration) have been used to record physiological sleep. ECG and respiration were the principal factors used to measure the ANS activity. EEG was used as a measure of the CNS activity. EEG was recorded according to the 10-20 international electrode placement system, with a sampling rate of 256Hz. While, EOG and EMG were recorded only to help in the classification of sleep states.

EEG:

The central area of the brain (C3 and C4) is known to be responsible for the generation of spindles and K-complexes and the occipital area (O1 and O2) for alpha activity and hence were our choice for analysis. This choice also gives us the information to study the two most characteristic parts of left and right hemispheres of the brain for the sleep activity. All the signals were pre-treated to reduce the artifacts. The EEG signals were pre-treated with a Rectangular High pass (RHP) of 0.1Hz. The obtained signals were then clipped off the high peaks (artifacts) and then applied a Rectangular Low

The recordings were obtained with the Deltamed Coherence 3 NT hardware-software device, which includes upto 19 channels for EEG and supplementary channels for ECG, EMG and Respiration. Electrodes used were either scalp or surface electrodes. The digitised results were then converted into ASCII format by an inbuilt software provided by the same manufacturer, and hence was compatible with the other softwares used in our analysis. The signals contained 50Hz noise and had to be pre-treated.

Data Analysis:

The signals were classified according to the standard methods [Bil94]. For our analysis, we took into consideration only four EEG electrodes (C3, C4, O1, O2), ECG and Respiration signals.

The recordings were classified manually, visualising the analog signals directly with the help of Coherence 3NT (a tool from the Deltamed Software), for the different states of sleep. Deltamed also provides a notch filter and other filtering options to get a better view of the signals and for reducing the artefacts, to obtain a better visual analysis.

The continuous polysomnography and observation of the behaviour (or video recording) are essential for the definition of different states of sleep and awake state in children. The different physiological signals required to describe the sleep states [Zea01], were then cut according to the different states of sleep and processed separately for different frequency bands. The duration of each state was carefully chosen to be characteristic of that particular state and with the least number of artefacts and disturbances each with a duration of 200 – 300 secs approximately.

Dataplore, a software tool designed for the analysis of signals and time series data by Datan Software & Analyse GmbH, Germany, is used for further analysis of the acquired signals. pass (RLP) of 40Hz, finally subsampled by a factor of two. Clipping the signal after high pass filtering enables to get rid off the artifacts and also resulted in higher signal to noise ratio compared to that of the band pass filtered signal. This was checked by performing the Fast Fourier transform (FFT) and also the amplitude spectrum of the two signals as can be seen from the following figure1. At the top is the original signal, in middle is that obtained by using a bandpass filter and the bottommost is that obtained by using the clipping technique and it shows the removal of artefacts effectively after 40Hz.

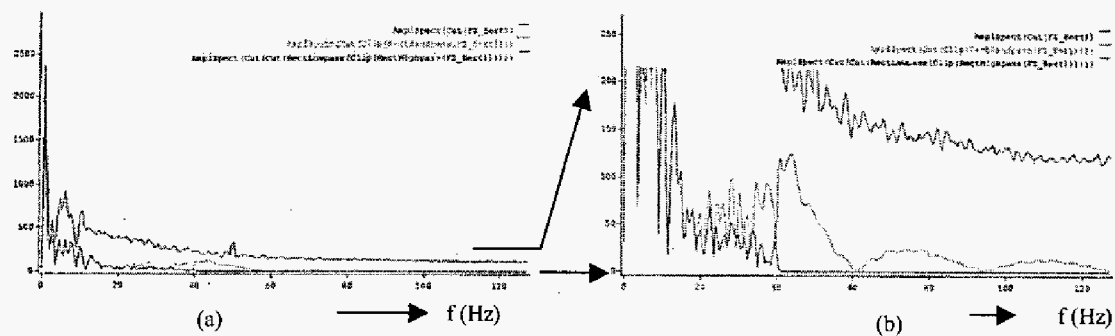


Figure 1: Amplitude spectrum of an EEG signal to compare the different types of filters. (a) complete view (b) detailed view.

The bandwise local mean power density was calculated for each electrode signal. This is obtained by calculating the Momentary band power (MBP) time series for each sleep state. The MBPs of each state were calculated for the six

frequency bands: Delta (0.5-3), Theta (3.5-7), Alpha1 (7.5-11), Alpha2 (11.5-13), Beta1 (13.5-20), and Beta2 (20.5-31.5) for the EEG signals (Figure2).

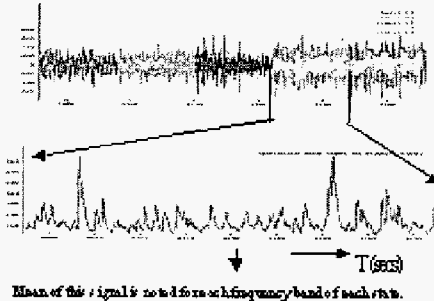


Figure 2: Shows the 5 sleep states and the calculation of momentary band power for each band of frequency and each sleep state – here is an example for alpha 2 band during state 3.

The four moments: Mean, Standard deviation, Skewness and Kurtosis of MBP and the kurtosis of the original signal were noted. The mean values of the MBP of EEG (O1, O2, C3, C4) signals were noted for each frequency band of each state. These mean values were plotted against the time scale for the entire sleep-wake cycle for each frequency series of each signal. This was useful to study the physiological changes occurring during the evolution of sleep. These values were finally normalised for all the subjects state-wise for each frequency band for each signal for different subjects.

state-wise i.e., the O1 and C3 values were added up and normalised to get one value for each state. And similarly C4 and O2 were normalised. These values were then plotted and compared to see how each side of the brain activity changes during the wake-sleep cycle. Graphs were drawn for the mean value of each state to study the changes in brain activity during the whole wake-sleep cycle for each frequency band. The other 3 moments were obtained only for 3 subjects and showed no significant results and hence were ignored later.

The normalisation was done by dividing each value of each frequency by the sum of that particular frequency in the states of sleep. The mean values for each frequency band and the standard deviation of these normalised values were also calculated finally to study the evolution of the activity of each signal as the subject enters the state of deep-sleep from the awake state. The left and right EEG signals were normalised

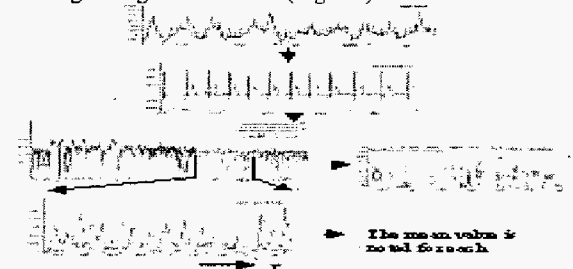
The cross correlations between the two EEG signals of the left and right side of the brain, i.e. O1–O2 and C3–C4 was performed and their values at zero were noted from the resulting signal. These cross correlation coefficients were plotted as a function of the sleep-wake cycle for each of the six frequency band series. This normalisation was also done to study if there are any characteristic differences between the left and right sides of the brain [Gue95].

ECG:

The ECG signal was filtered with a Rectangular band pass (RBP) of (1-40) Hz to remove the 50Hz frequency artifacts. Clipping technique was not employed here as our main interest lies in the R peaks.

time series was calculated for the reciprocal of R-R distance for the LF (0.05-0.15) Hz and HF (0.15-0.4) Hz frequency bands for each sleep state. The four moments: Mean, Standard deviation, Skewness and Kurtosis of MBP and the kurtosis of the original signal were noted (Figure3).

Calculation of the R-R distance: The R-R intervals distance (peak to peak) time series was calculated by choosing the appropriate window size and the threshold value from the ECG signal for each subject and sleep state. The reciprocal of it was obtained to get the R-R distance in the frequency band to be able to compare with the other acquired physiological signals and was subsampled by a factor of two. This was done to obtain the heart rate variability (HRV) and is useful for further analysis.



The multiscale TFD was calculated for the low frequency and high frequency bands. This was done to determine the characteristic frequencies of the LF and HF bands. The MBP

Figure 3: ECG analysis, filtering and reciprocal of the peak to peak distance for the 5 states of surveillance, momentary band power for LF and HF

The first moment (mean) values of the above MBP signals were noted for each frequency band of each state. These mean values were plotted against the time scale for the entire sleep-wake cycle for each frequency series of each signal. This was useful to study the physiological changes occurring during the evolution of sleep. These values were finally normalised for all the subjects state-wise for each frequency band for different subjects. The normalisation was done by dividing each value of each frequency by the sum of that particular frequency in the states of sleep. The mean values for each frequency band and the standard deviation were also calculated finally to study the evolution of the activity of each signal as the subject enters the state of deep sleep from the awake state. Graphs were drawn for the mean value of each state to study the changes in cardiac activity during the sleep cycle for each frequency band. The other three moments were obtained only for 3 subjects.

RESP:

A RHP of 0.1Hz was applied to the acquired RESP signal, clipped the resulting signal off the high artifacts and then applied a RLP of 10Hz and subsampled by a factor of 2. The multiscale TFD was obtained for the frequency band of 0 – 10 Hz to characterise the frequency region in which the respiration activity occurs. The MBP time series was thus calculated for the characteristic frequency band of (0.2-0.4) Hz for each state of surveillance.

The four moments: Mean, Standard deviation, Skewness and Kurtosis of MBP and the kurtosis of the original signal were noted just as in the case of EEG. The mean value (first moment) of the above MBP time series was obtained for the different states of sleep for different subjects and the corresponding graphs were drawn. These values were finally normalised for all the subjects state-wise for the above MBP time series for different subjects. The normalisation was done by dividing each value of each frequency by the sum of that particular frequency in the states of sleep. The mean values of each frequency band and the standard deviation were calculated finally to study the evolution of the activity of each signal as the subject enters the state of deep sleep from the awake state. Graphs were drawn for the normalised mean value to study the changes in the respiration activity during the wake-sleep cycle for each frequency band. The other 3 moments were obtained only for 3 subjects.

Interaction between ECG and Respiration:

The cross correlation between the MBP of R-R distance and MBP of RESP was performed and the graphs were drawn for the LF and HF frequency band series (Figure4).

Interaction between the ANS and CNS:

The cross correlation between the MBP (2 frequency bands) of the reciprocal of R-R distance (ECG) and MBP (6 frequency bands) of EEG signals was performed and the respective graphs were drawn for the six frequency band series' (Figure4).

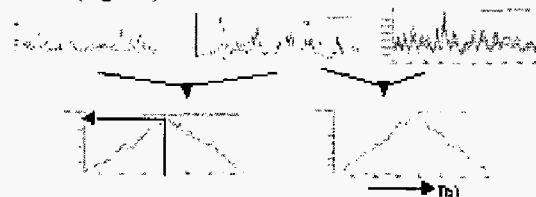


Figure 4: Cross-correlation method between MBP of EEG, ECG and RESP

Normalisation:

The mean of the correlation coefficient values for each frequency band between each pair of correlated signals was calculated for each frequency band and the corresponding

graphs were obtained. The normalisation was done by calculating the mean value of the cross correlation coefficient for each pair of signals for each frequency in all the states put together as the correlation coefficient obtain using the Dataplore software is itself already normalised. The normalisation was done frequency wise and then state-wise for each of the different physiological signals studied.

3. RESULTS:

The classification of the different states of sleep has been done as described in methods. Statistical data concerning the duration of each sleep cycle during the first awake-sleep transition obtained has been summarised in the table1 below. This table gives the mean duration, the standard deviation and the duration of each of the four sleep states. For our subjects, we found that states 1 and 3 are relatively short and almost imilar in duration for all subjects while the duration of states 2 and 4 are much longer and show a high inter-subject variability.

Sleep states	Mean Duration (min)	Standard deviation (min)	Duration (min)
State1	4.19	2.42	1.77 – 6.61
State2	12.5	8.88	3.62 – 21.38
State3	5.38	1.69	3.69 – 7.07
State4	22.88	12.47	10.41 – 35.35

Table 1: Analysis of the duration of different phases of slow sleep.

The Multiscale time-frequency distribution of the peak to peak of ECG for the frequency band of (0.01 – 0.5) Hz in the children examined shows that the main activity of cardiac variability occurs for our subjects also in the well known range of the frequency band between (0.05-0.4) Hz, which can hence be divided as common use just as in the case of adults as low frequency band of (0.05-0.15) Hz and high frequency band of (0.15-0.4) Hz, an indicator of the parasympathetic activity. This has been done for the whole wake-sleep cycle analysis (120 – 180 secs) (Figure5).

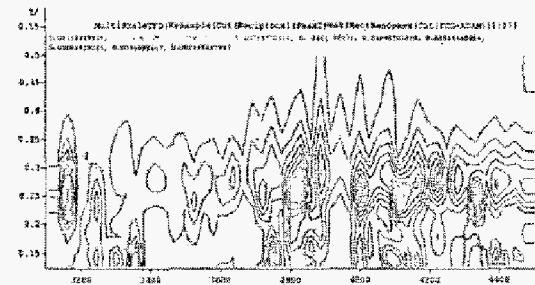


Figure 5: MBP of the peak to peak of ECG for the band (0 – 0.5) Hz

The momentary band power of peak to peak of ECG, EEG and RESP during slow sleep (state3) gives a measure of the activity occurring in each frequency band at a particular instant of time for each sleep state for each signal. In this manner, we created 1080 time series representing a duration of about 162 000 seconds. This is used as the basis for further analysis.

The mean activity of each region of the brain for each state or each frequency band series has been obtained. The mean value (8 subjects) of delta activity increases during sleep and Beta2 decreases while the activity of the intermediate frequencies look like a transition between the two frequency bands of O1 and O2. C3 and C4 follow almost a similar trend or the different frequencies except in state 2 where it is always a bit higher relatively. The powers in the higher

frequency bands are higher in awake state and decrease as they move on to State4. Analysis justified the division of the two frequency bands - alpha1 and alpha 2 into two sub-bands. Both of the bands have lowest power during state1. Powers of alpha1 and delta increase while that of alpha2 and Beta2 decrease during sleep transition.

The mean values of each state series were also plotted as a function of each frequency band. The trend, which it follows, suggests that there is a balance of the activities taking place during awake-sleep transition i.e., the power of activity in awake state shows a gradual increase for the increase in frequency while the state 4 shows a decrease and the intermediate states show a transition between the two extreme states of sleep. The mean activity in the bands alpha1, alpha2 and beta1 are not modified much during the states of sleep. This is true for the cerebral regions studied. Each figure shows the mean activity for each region of the brain and each frequency band. All frequency bands show this transition except alpha2, which behaves a bit differently from the rest and seems to be relatively stable with less change for different states of sleep. This is observed with the occipital regions (O1 and O2) and also in the central regions (C3 and C4) for different frequency bands. Nevertheless, when we consider the state2, one can observe a certain increase in the high frequency bands and is high during awake and decreases as the subject enters state 4.

The average activity in the left and right sides of the brain did not show any significant differences in activity on the different sides but showed a constant increase in activity during the wake-sleep cycle except for a slight decrease in state1 (Table 2 and Figure 6).

Table 1: Activities of left and right hemispheres

State	A	S1	S2	S3	S4
Left	0,1196	0,0872	0,1526	0,2366	0,404
Right	0,1325	0,106	0,1524	0,2313	0,3777

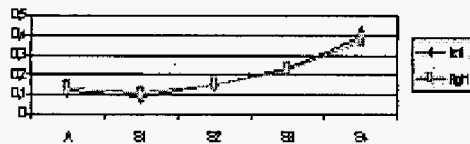


Figure 6: Activities of the left and right hemispheres

The cross correlation between the activity of the two sides of the brain is relatively very high as can be seen from the following figures. The correlation between C3-C4 develops similarly for the different frequency bands for the wake-sleep transition achieving a relative minimum for state 2 and then again increases for state3 and 4. In contrast, the correlation between O1-O2 develops individually for each frequency band for the awake-sleep transition and is not homogeneous. The cross correlation between the low frequency cardiac activity and the brain activity was found to be higher in state3 than in the other states. The high frequency correlation of the cardiac and brain activity did not develop similarly. The cross correlation between R-R distance (ECG) and RESP was found to increase progressively during the awake-sleep transition achieving a maximum during state3 and then decreasing again for state4.

4. DISCUSSION AND CONCLUSION

Spectral analysis is most frequently used in signal treatment due to its advantage of a principally infinite frequency

resolution [Tet03], [Otz97], [Wad95]. Anyway it does not provide appropriate numerical values to describe, e.g. sleep states. For this purpose, it has to be split into different frequency bands for further analysis as required. So, here we chose the MBP, which can be taken for a digitisation of the power spectrum. It gives the power of the signal in a particular frequency band in a chosen interval of time and provides a finite value, characterizing the activity of the underlying subsystem for each instant of time in a given frequency band. Applying this approach, we end up with time series characterizing the time resolved activity of the subsystems. These time series can then be used for further investigation on the interrelationship between different systems.

Another method developed during our work, is concerned with the reduction of artifacts. We have shown by the amplitude spectrum, that the usage of sequence:

high pass – clip – lowpass filtering

proved to be much more effective than the usual bandpass filtering to remove the unwanted frequencies and artifacts.

If one takes into account the usual frequency bands for the subdivision of the EEG activity, we recommend that the alpha activity should be divided into two sub bands: alpha 1 and alpha 2. Previous studies [Joa00] have shown that the mean logarithmic spectral density for the alpha band increase during the sleep transition. Nevertheless, on dividing the alpha band into alpha 1 and alpha 2, we have observed that this is true for alpha 1 band alone, while the alpha 2 frequencies have a tendency to decrease in state 4.

The mean activity of the central region of the brain (C3, C4) in state2 is relatively higher than the other states of sleep and confirms the arousal of spindles from that region that are known to be very characteristic of state 2 of sleep.

The linear regression analysis of the obtained results showed that the variations in the activities in different frequency bands are very feeble during state 2. According to other researchers, the correlation dimensions decrease from the 'awake' state to sleep stages 1-3 and increased during rapid eye movement (REM) sleep. These results were seen during each sleep cycle. In each sleep cycle, the correlation dimensions decrease for slow wave sleep, and increase for REM sleep [Kob99]. Alpha waves occurred in fronto-central areas during slow wave sleep, migrated to posterior areas during REM sleep, and were localized in occipital areas during intra-sleep awakenings [Ehr00].

The correlations between EEG activities of identical frequencies but of different topographies were highly positive during sleep, while the correlations between activities of different frequencies at the same site on the scalp varied according to sleep states and frequencies [Ban83]. In the same manner, we observed that the correlation between the left and right hemispheres of the brain for the central regions varies with the different states of sleep. Also, this correlation was found to be relatively lower in state2 for central regions while it increases during states 3 and 4 for all frequency bands.

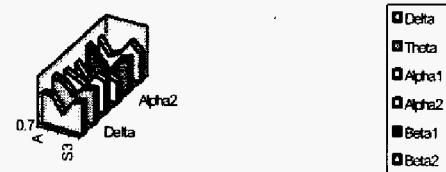


Figure 7: Cross correlation between the left (C3) and right (C4) hemispheres

State 2 presents some particular characteristics, with regard to results presented. In this state, we observe less variability of frequencies, diminution in correlation between the two hemispheres and decrease in correlation of different cerebral and cardiac activities. Moreover, in state 2, the influence of parasympathetic and sympathetic activity on the cardiac activity appear to be in equilibrium while during awake and state 1, the sympathetic activity dominates and during states 3 and 4, it is the parasympathetic activity which dominates. Thus highlighting the influence of sleep states on the ortho-parasympathetic balance. We have to consider for further study, the relations that may exist between the frequencies of cerebral activities and the ortho-parasympathetic balance in the measure or evolution of certain cerebral activities in certain frequency bands, which may be correlated with the cardiac variability.

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